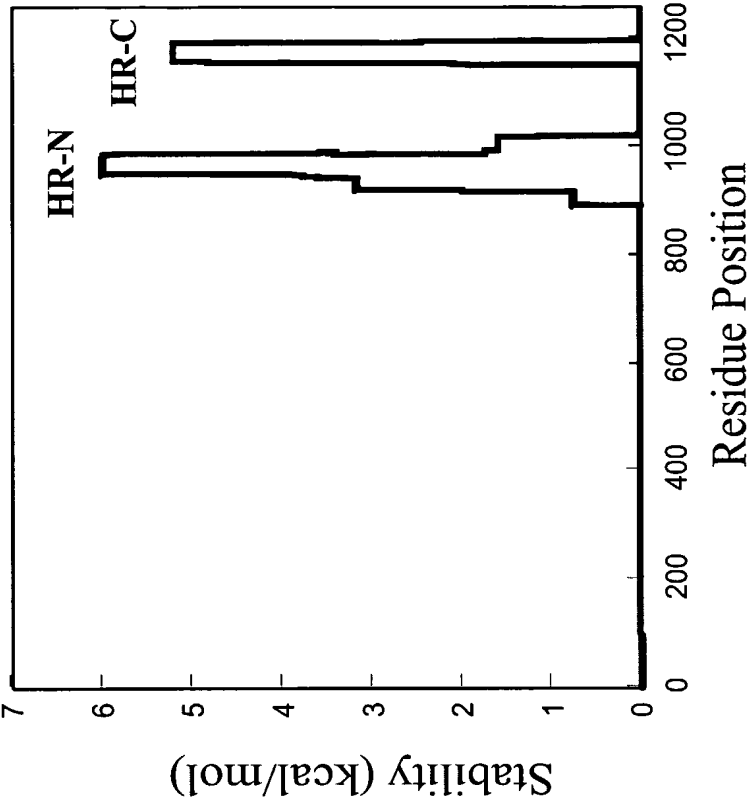


A



B

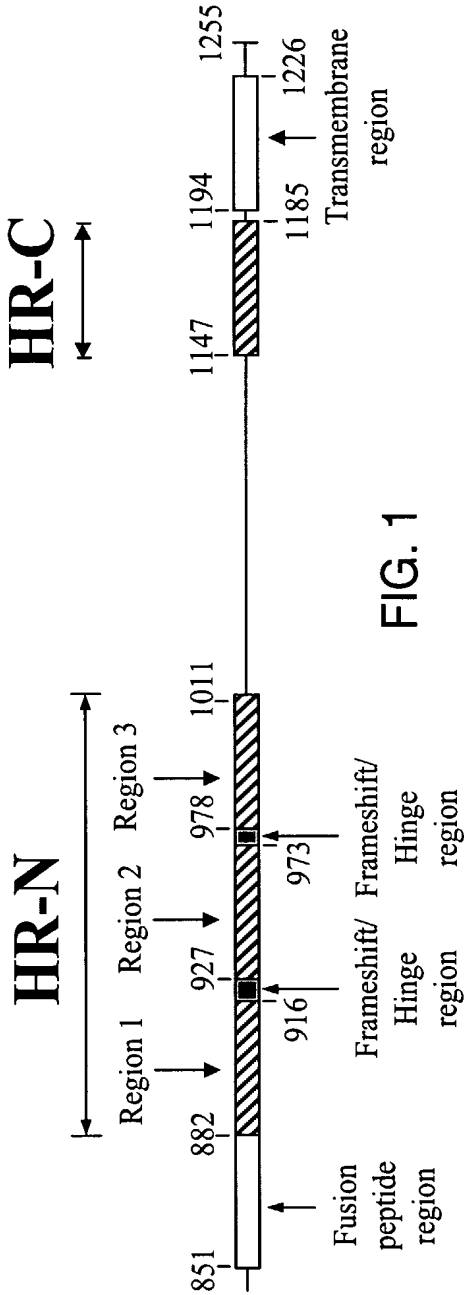


FIG. 1

3/23

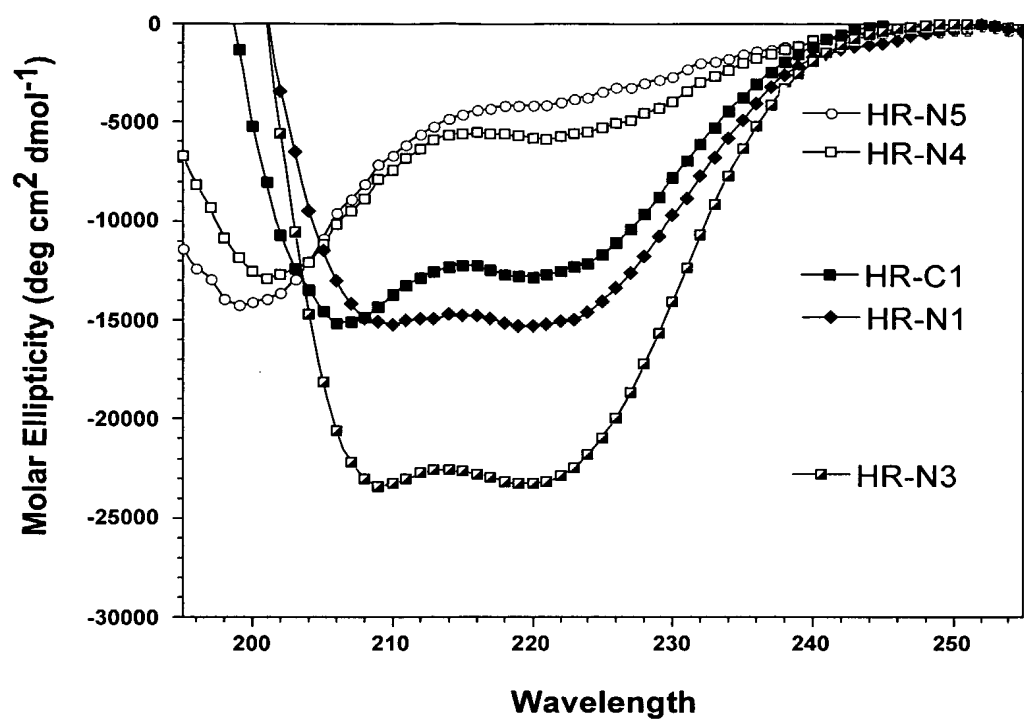
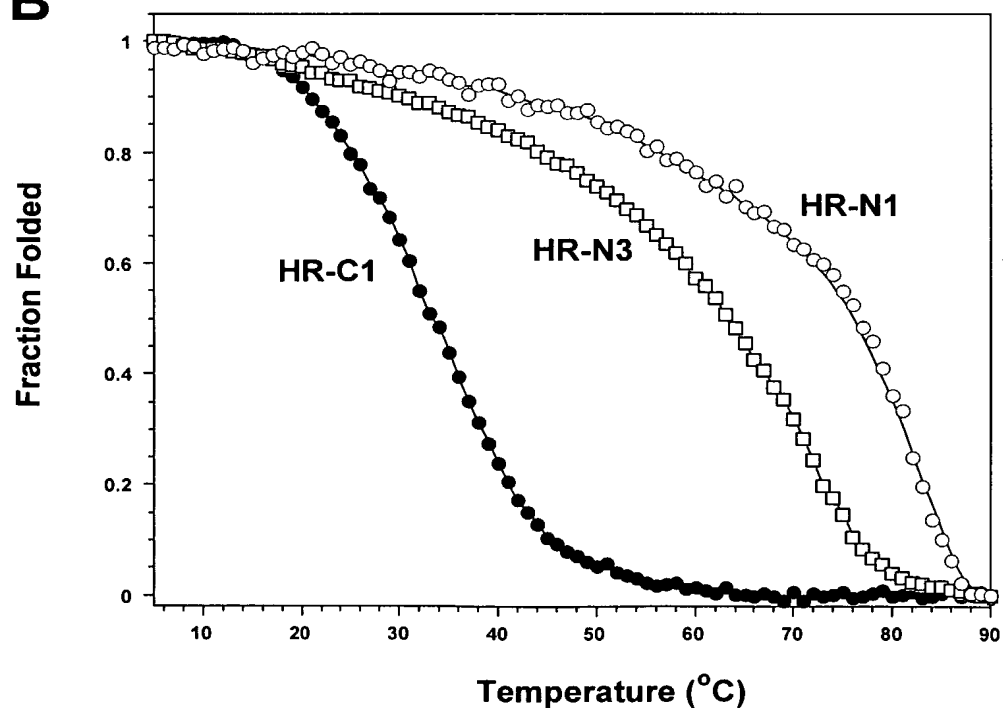
A**B**

FIG. 3

4/23

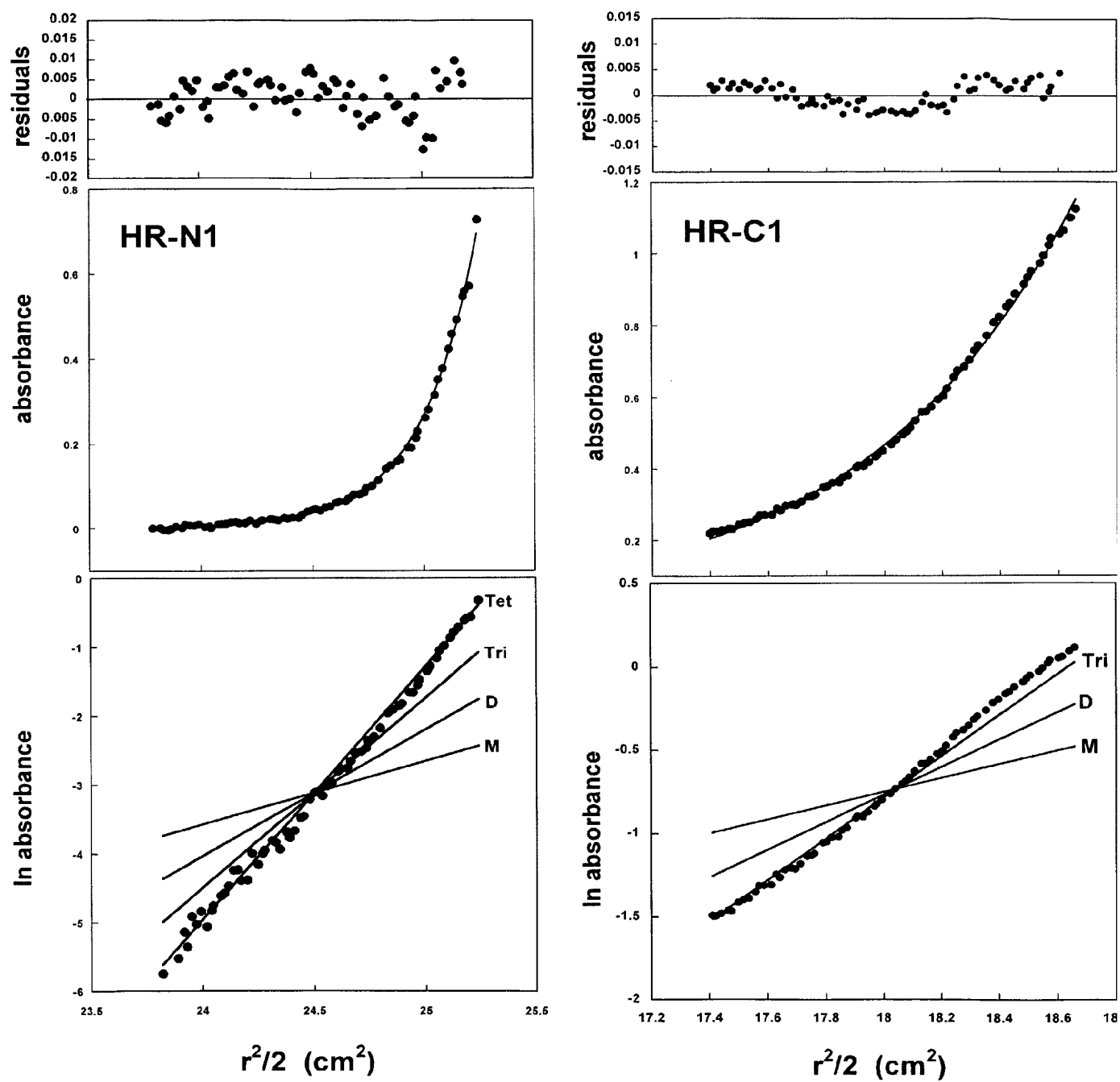


FIG. 4

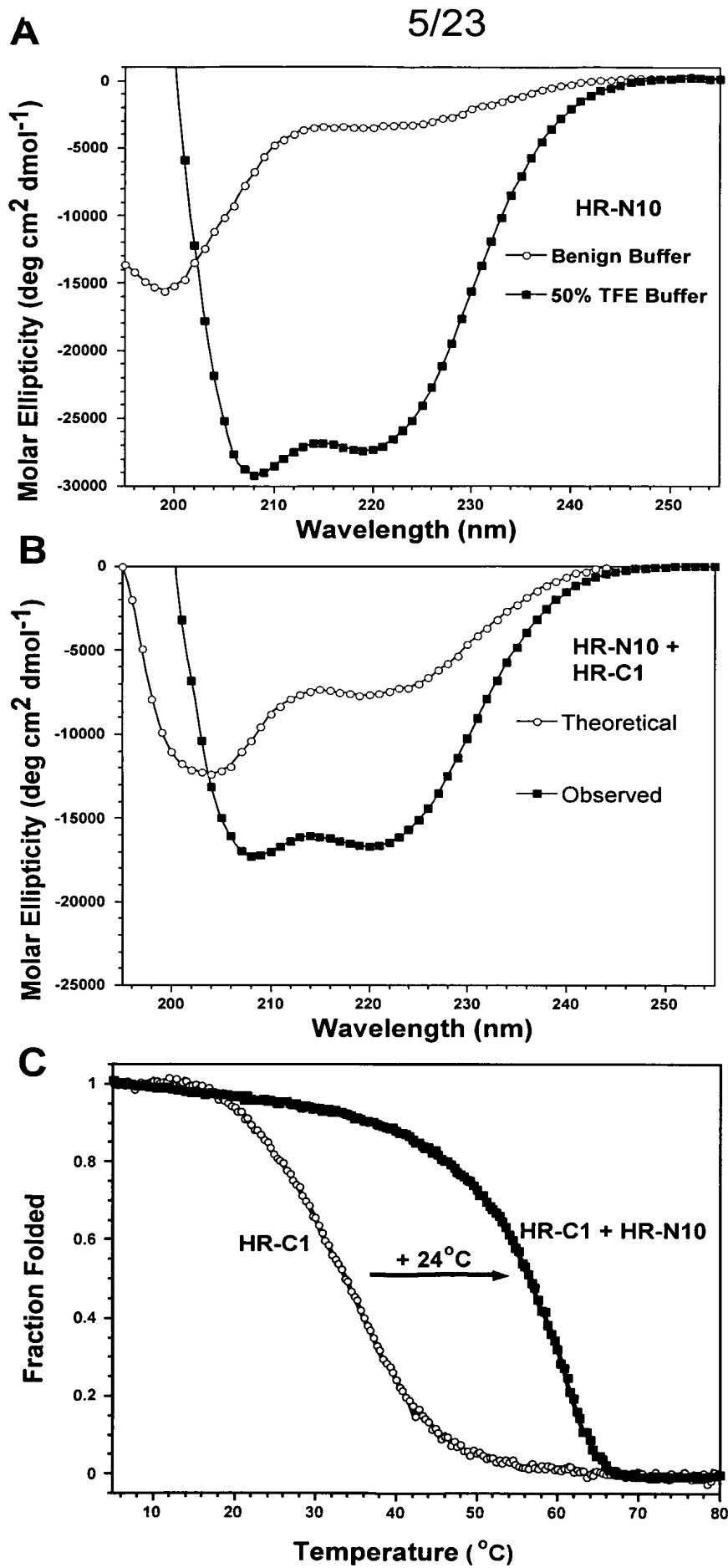


FIG. 5

6/23

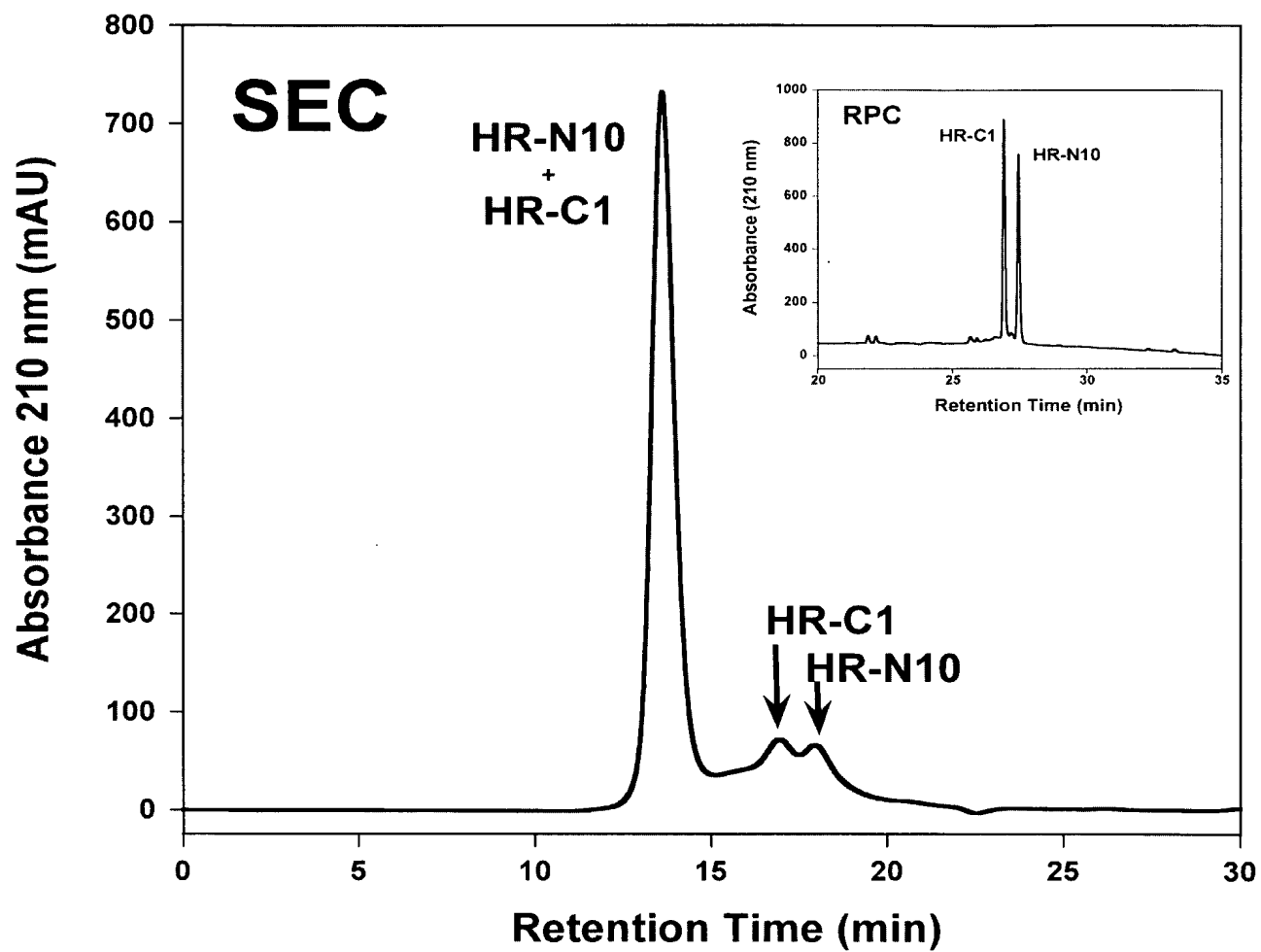


FIG. 6

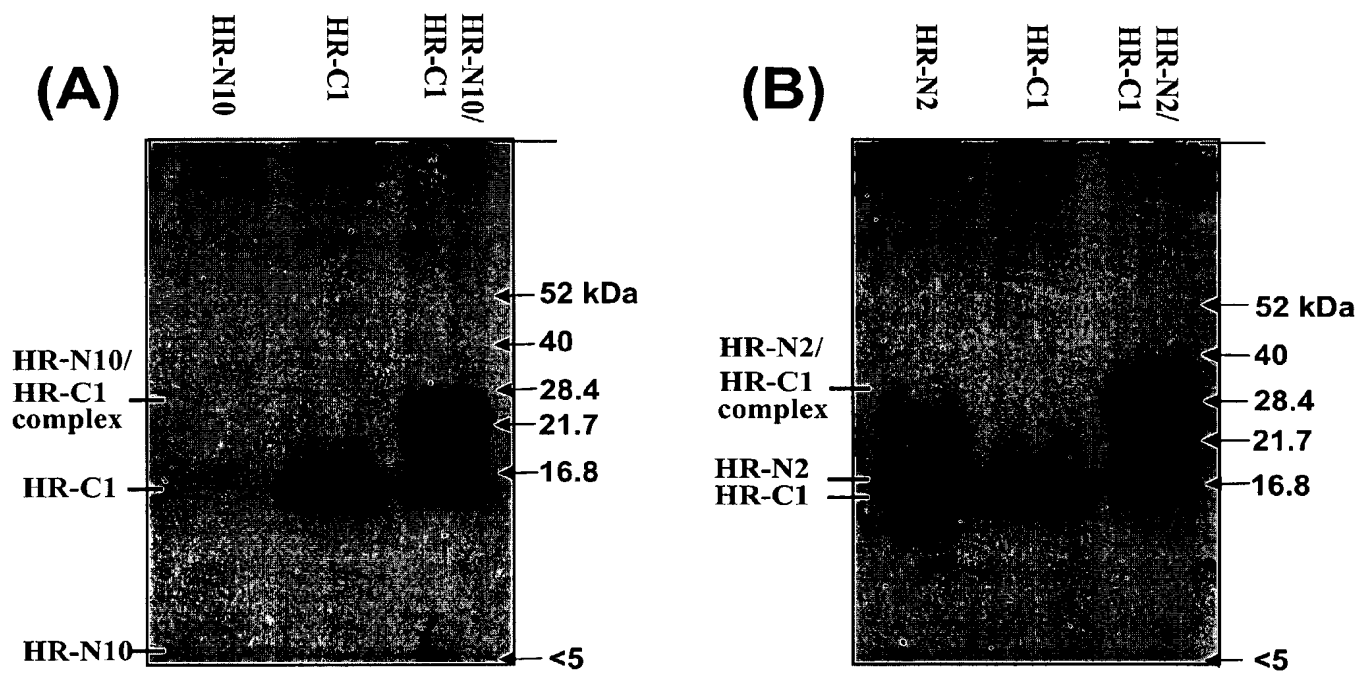


FIG. 7

8/23

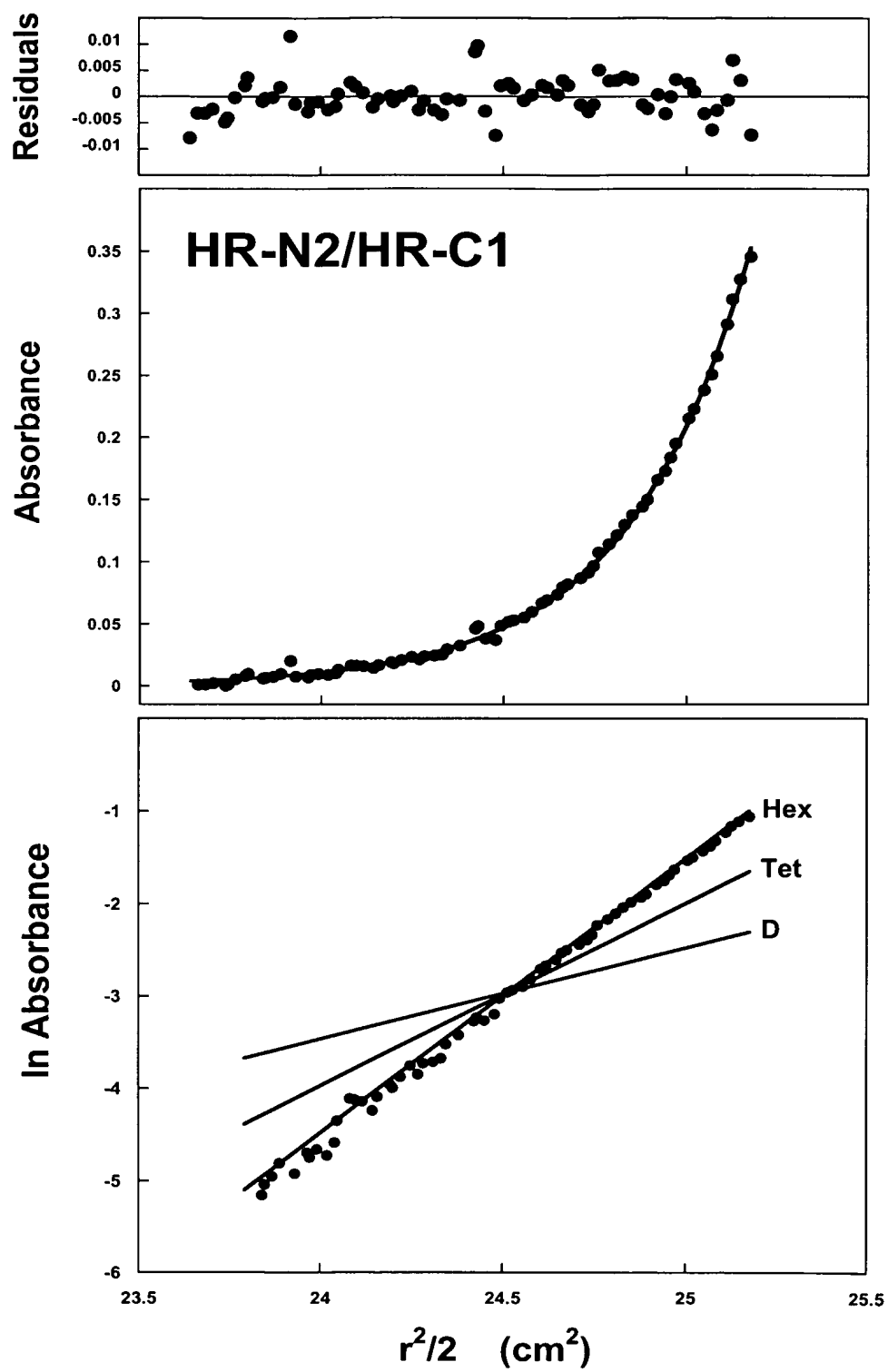


FIG. 8

9/23

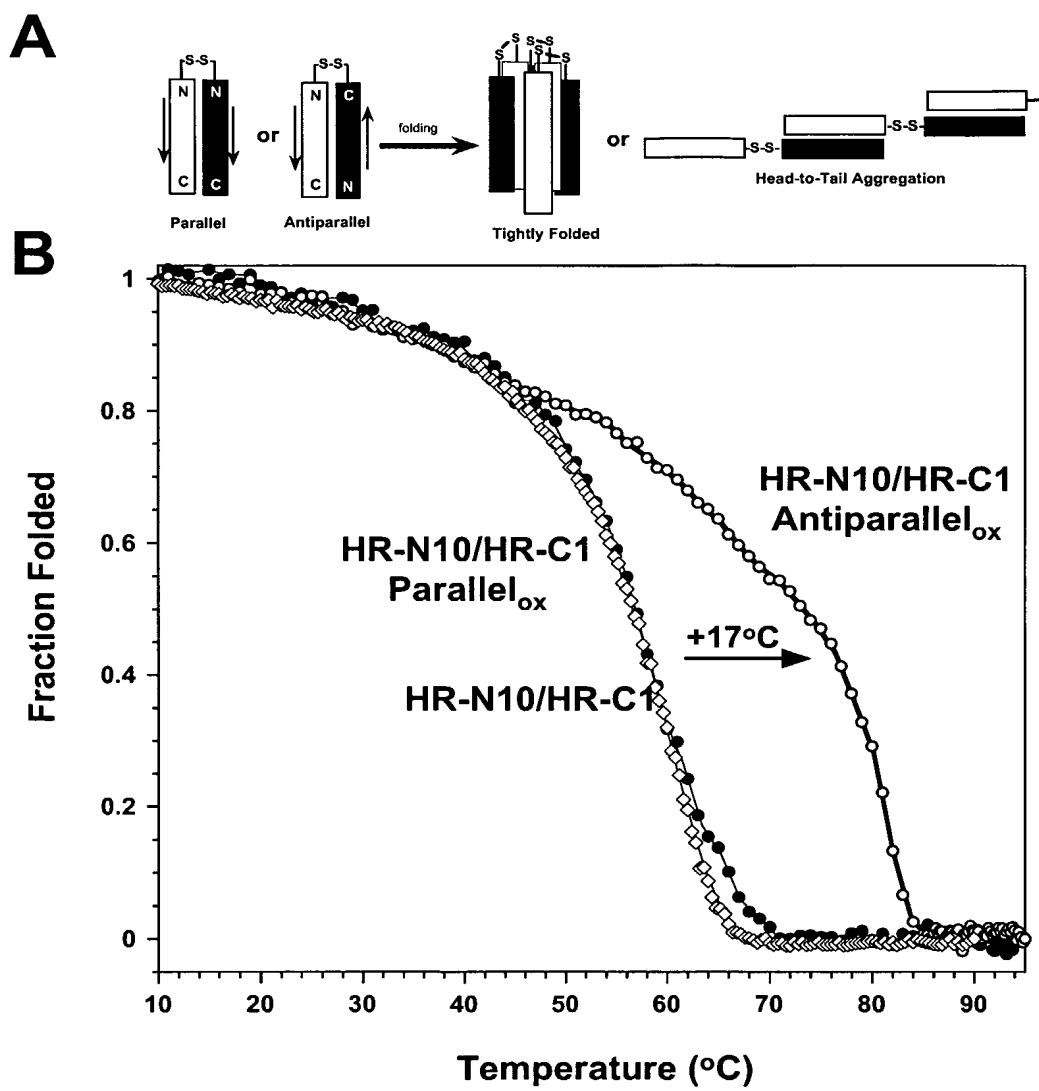


FIG. 9

10/23

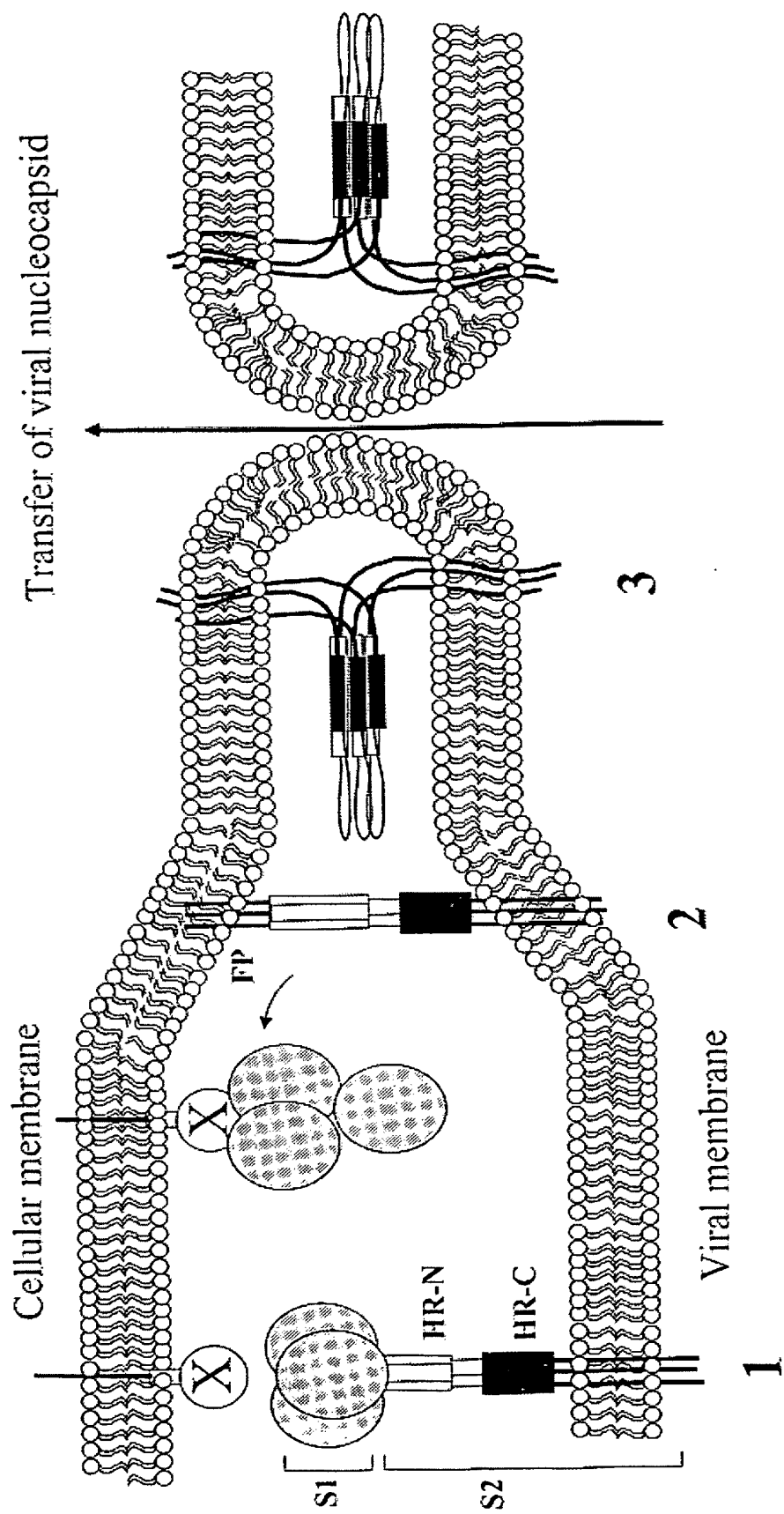


FIG. 10

11/23

HR-N (916-950)

(native)

Ac-IQESLTTTSTALGKLQDVVNQNAQALNTLVKQLSS-amide

(Ala, Lys and Arg substituted)

Ac-IQAALTKTSAALGKLQAAVNRNAAALNKLVKALSS-amide

(Aib=B substituted)

Ac-IQESLTBTSTALGKLQDVVNBNAQALNBLVKQLSS-amide

(Dxg=Z substituted)

Ac-IQESLTZTSTALGKLQDVVNZNAQALNZLVKQLSS-amide

HR-C (1151-1185)

(native)

Ac-ISGINASVVNIQKEIDRLNEVAKNLNESLIDLQEL-amide

(Ala, Lys and Arg substituted)

Ac-IAAINKSVAAIQKEIARLNEVAKALNASLIRLQAL-amide

(Aib=B substituted)

Ac-ISGINBSVVNIQKEIDRLNBVAKNLNBSLIDLQEL-amide

(Dxg=Z substituted)

Ac-ISGINZSVVNIQKEIDRLNZVAKNLNZSLIDLQEL-amide

FIG. 11

12/23

HR-N (916-950)

Ac-IQESLTTTSTALGKLQDVVNQNAQALNTLVKQLSS-amide

1 i,i+4 lactam bridge

Ac-IQESLTTTSTALGKLQEVVNKNAQALNTLVKQLSS-amide

**2 i,i+4 lactam bridge**

Ac-IQESLTETSTKLGKLQDVVNQNAQALNELVKKLSS-amide

**1 i,i+7 bridge**

Ac-IQESLTTTSTALGELQDVVNENAQALNTLVKQLSS-amide

**HR-C (1151-1185)**

Ac-ISGINASVVNIQKEIDRLNEVAKNLNESLIDLQEL-amide

1 i,i+4 lactam bridge

Ac-ISGINASVVNIQKEIERLNKVAKNLNESLIDLQEL-amide

**2 i,i+4 lactam bridge**

Ac-ISGINESVVKIQKEIDRLNEVAKNLNESLIKQLQEL-amide

**1 i,i+7 bridge**

Ac-ISGINASVVNIQEEIDRLNEVAKNLNESLIDLQEL-amide



= covalent bond

FIG. 12

HR-N (916-950)

Ac-IQESLTTTSTALGKLQDVVNQNAQALNTLVKQLSS-amide

(Ile and Leu substituted into the hydrophobic core)

Ac-IIESLTTTITALGKLIDVLNQNIQALNTLIKQLSS-amide

HR-C (1151-1185)

Ac-ISGINASVVNIQKEIDRLNEVAKNLNESLIDLQEL-amide

(Ile substituted into the hydrophobic core)

Ac-ISGINASIVNIQKEIDRLNEVIKNLNESLIDLQEL-amide

FIG. 13

14/23

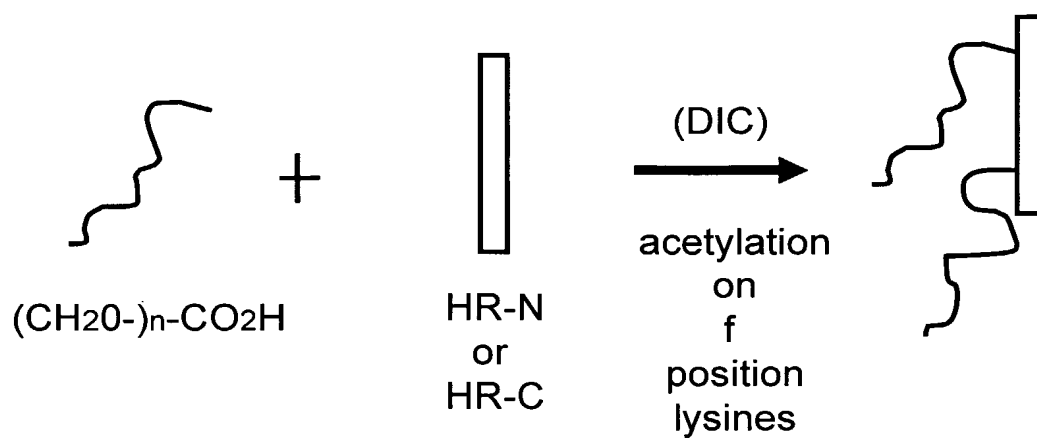


FIG. 14

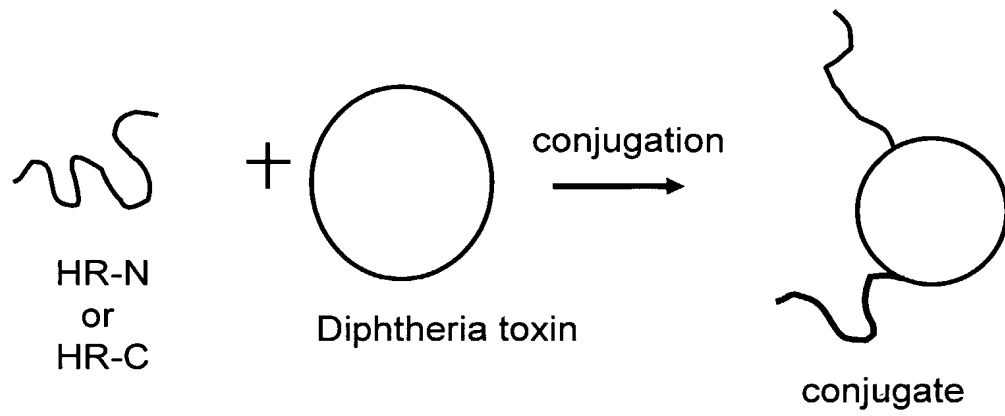


FIG. 15

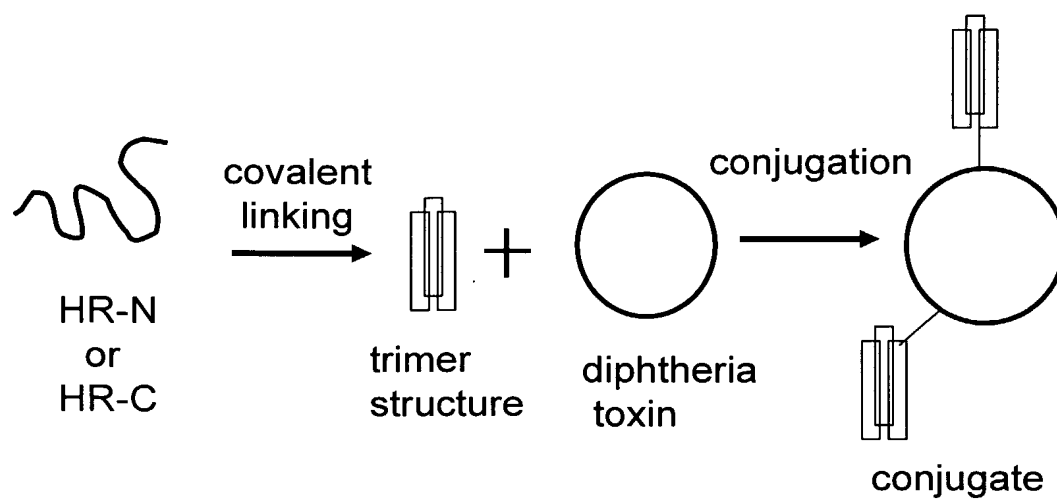


FIG. 16A

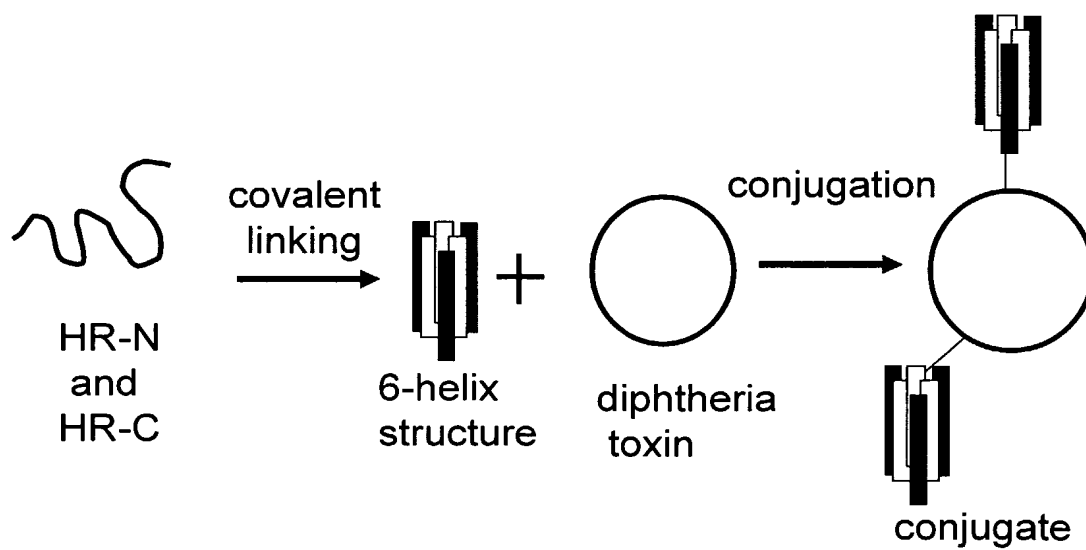


FIG. 16B

17/23

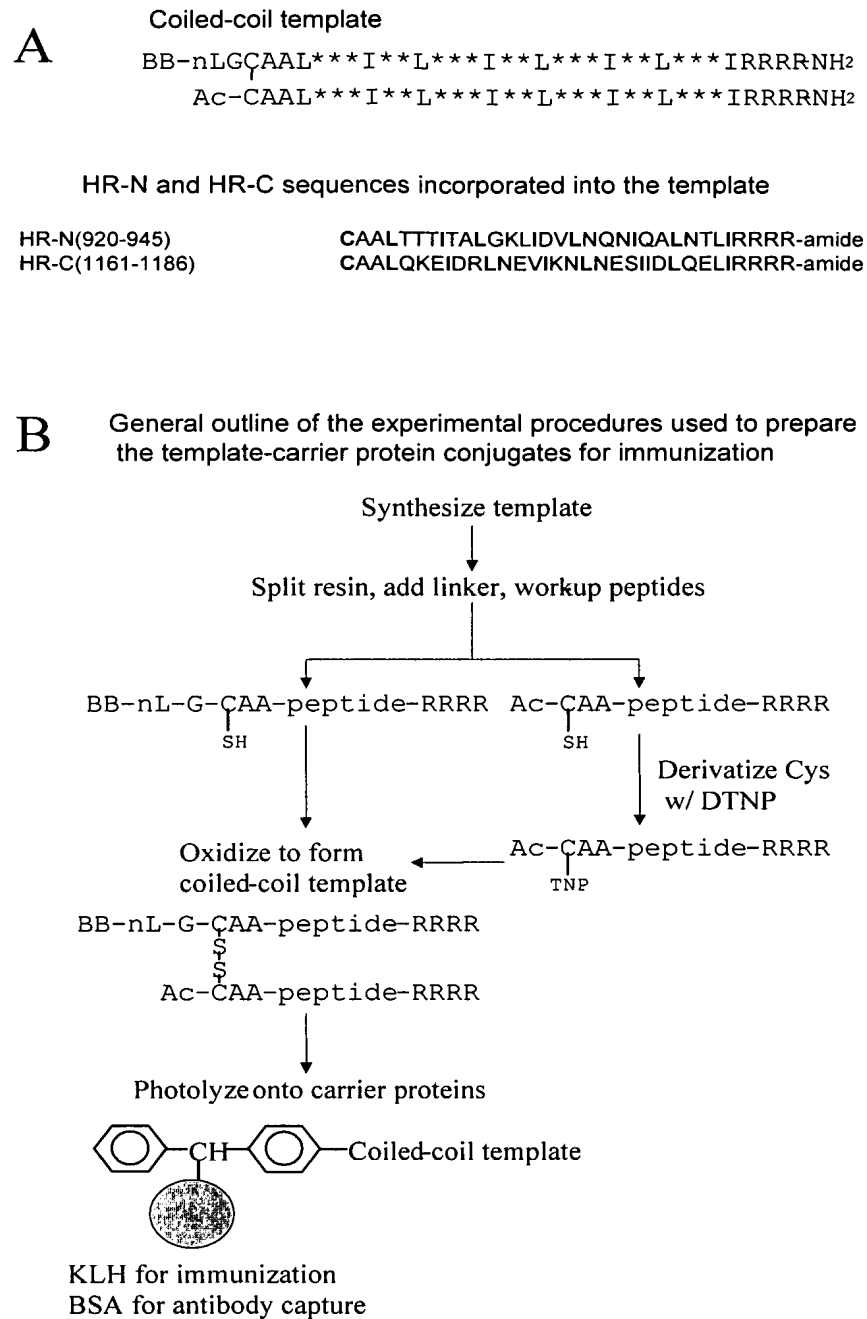


FIG. 17

18/23

HR-N peptides, HR-N1 to HR-N17.

Nucleotide sequences for SARS peptides. The amino acid region is shown in brackets.

HR-N1 (882-973)

ATGCAAATGGCATATAGGTTCAATGGCATTGGAGTTACCCAAAATGTTCTCTATGAGAACCA
AAAACAAATCGCCAACCAATTTAACAAGGCGATTAGTCAAATTCAGAATCACTTACAACAA
CATCAACTGCATTGGGCAAGCTGCAAGACGTTGTTAACCAGAATGCTCAAGCATTAAACACA
CTTGTTAAACAACTTAGCTCTAATTTTGGTGCAATTTCAAGTGTGCTAAATGATATCCTTTC
GCGACTTGATAAAGTCGAGGCGGAGGTA

HR-N2 (916-973)

ATTCAAGAATCACTTACAACAACATCAACTGCATTGGGCAAGCTGCAAGACGTTGTTAACCA
GAATGCTCAAGCATTAAACACACTTGTTAAACAACTTAGCTCTAATTTTGGTGCAATTTCAA
GTGTGCTAAATGATATCCTTTCGCGACTTGATAAAGTCGAGGCGGAGGTA

HR-N3 (927-973)

TTGGGCAAGCTGCAAGACGTTGTTAACCAGAATGCTCAAGCATTAAACACACTTGTTAAACA
ACTTAGCTCTAATTTTGGTGCAATTTCAAGTGTGCTAAATGATATCCTTTCGCGACTTGATA
AAGTCGAGGCGGAGGTA

HR-N4 (974-1011)

CAAATTGACAGGTTAATTACAGGCAGACTTCAAAGCCTTCAAACCTATGTAACACAACAAC
AATCAGGGCTGCTGAAATCAGGGCTTCTGCTAATCTTGCTGCTACTAAAATG

HR-N5 (882-916)

ATGCAAATGGCATATAGGTTCAATGGCATTGGAGTTACCCAAAATGTTCTCTATGAGAACCA
AAAACAAATCGCCAACCAATTTAACAAGGCGATTAGTCAAATT

HR-N6 (888-922)

TTCAATGGCATTGGAGTTACCCAAAATGTTCTCTATGAGAACCACAAAACAAATCGCCAACCA
ATTTAACAAGGCGATTAGTCAAATTCAGAATCACTTACAACA

HR-N7 (895-929)

CAAAATGTTCTCTATGAGAACCACAAAACAAATCGCCAACCAATTTAACAAGGCGATTAGTCA
AATTCAGAATCACTTACAACAACATCAACTGCATTGGGCAAG

FIG. 18A

19/23

HR-N8 (902-936)

CAAAAACAAATCGCCAACCAATTTAACAAGGCGATTAGTCAAATTCAAGAATCACTTACAAC
AACATCAACTGCATTGGGCAAGCTGCAAGACGTTGTTAACCAG

HR-N9 (909-943)

TTTAACAAGGCGATTAGTCAAATTCAAGAATCACTTACAACAACATCAACTGCATTGGGCAA
GCTGCAAGACGTTGTTAACCAGAATGCTCAAGCATTAAACACA

HR-N10 (916-950)

ATTCAAGAATCACTTACAACAACATCAACTGCATTGGGCAAGCTGCAAGACGTTGTTAACCA
GAATGCTCAAGCATTAAACACACTTGTAAACAACCTTAGCTCT

HR-N11 (923-957)

ACATCAACTGCATTGGGCAAGCTGCAAGACGTTGTTAACCAGAATGCTCAAGCATTAAACAC
ACTTGTAAACAACCTTAGCTCTAATTTTGGTGCAATTTCAAGT

HR-N12 (931-965)

CAAGACGTTGTTAACCAGAATGCTCAAGCATTAAACACACTTGTAAACAACCTTAGCTCTAA
TTTTGGTGCAATTTCAAGTGTGCTAAATGATATCCTTTCGCGA

HR-N13 (938-972)

GCTCAAGCATTAAACACACTTGTAAACAACCTTAGCTCTAATTTTGGTGCAATTTCAAGTGT
GCTAAATGATATCCTTTCGCGACTTGATAAAGTCGAGGCGGAG

HR-N14 (945-979)

GTTAAACAACCTTAGCTCTAATTTTGGTGCAATTTCAAGTGTGCTAAATGATATCCTTTCGCG
ACTTGATAAAGTCGAGGCGGAGGTACAAATTGACAGGTTAATT

HR-N15 (952-986)

TTTGGTGCAATTTCAAGTGTGCTAAATGATATCCTTTCGCGACTTGATAAAGTCGAGGCGGA
GGTACAAATTGACAGGTTAATTACAGGCAGACTTCAAAGCCTT

HR-N16 (959-993)

CTAAATGATATCCTTTCGCGACTTGATAAAGTCGAGGCGGAGGTACAAATTGACAGGTTAAT
TACAGGCAGACTTCAAAGCCTTCAAACCTATGTAACACAACAA

HR-N17 (966-1000)

CTTGATAAAGTCGAGGCGGAGGTACAAATTGACAGGTTAATTACAGGCAGACTTCAAAGCCT
TCAAACCTATGTAACACAACAATAATCAGGGCTGCTGAAATC

FIG. 18B

20/23

HR-C peptides, HR-C1 to HR-C4

Nucleotide sequences for SARS peptides. The amino acid region is shown in brackets.

HR-C1 (1147-1185)

GATGTTGATCTTGGCGACATTT CAGGCATTAACGCTTCTGTCGTCAACATTCAAAAAGAAAT
TGACCGCCTCAATGAGGTCGCTAAAAATTTAAATGAATCACTCATTGACCTTCAAGAATTG

HR-C2 (1165-1185)

ATTGACCGCCTCAATGAGGTCGCTAAAAATTTAAATGAATCACTCATTGACCTTCAAGAATT
G

HR-C3 (1158-1185)

GTCGTCAACATTCAAAAAGAAATTGACCGCCTCAATGAGGTCGCTAAAAATTTAAATGAATC
ACTCATTGACCTTCAAGAATTG

HR-C4 (1151-1185)

ATTT CAGGCATTAACGCTTCTGTCGTCAACATTCAAAAAGAAATTGACCGCCTCAATGAGGT
CGCTAAAAATTTAAATGAATCACTCATTGACCTTCAAGAATTG

Amino acid sequence for SARS peptide HR-C1

HR-C1 (1147-1185)

DLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQEL

FIG. 19

HR-N

Nucleotide sequences for SARS peptides. The amino acid region is shown in brackets.

HR-N (882-1011)

ATGCAAATGGCATATAGGTTCAATGGCATTGGAGTTACCCAAAATGTTCTCTATGAG
AACCAAAAACAAATCGCCAACCAATTTAACAAGGCGATTAGTCAAATTCAAGAATCACTTAC
AACAACATCAACTGCATTGGGCAAGCTGCAAGACGTTGTTAACCAGAATGCTCAAGCATTAA
ACACACTTGTTAAACAACCTTAGCTCTAATTTTGGTGCAATTTCAAGTGTGCTAAATGATATC
CTTTCGCGACTTGATAAAGTCGAGGCGGAGGTACAAATTGACAGGTTAATTACAGGCAGACT
TCAAAGCCTTCAAACCTATGTAACACAACAATAATCAGGGCTGCTGAAATCAGGGCTTCTG
CTAATCTTGCTGCTACTAAAATG

FIG. 20

ATGTTTATTTTCTTATTATTCTTACTCTCACTAGTGGTAGTGACCTTGACCGGTGCACCACTTTTGATG
ATGTTCAAGCTCCTAATTACACTCAACATACTTCATCTATGAGGGGGTTTACTATCCTGATGAAATTTT
TAGATCAGACACTCTTTATTTAACTCAGGATTTATTTCTTCCATTTTATTCTAATGTTACAGGGTTTCAT
ACTATTAATCATACGTTTGGCAACCCTGTCATACCTTTTAAAGGATGGTATTTATTTTGCTGCCACAGAGA
AATCAAATGTTGTCCGTGGTGGGTTTTTGGTCTACCATGAACAACAAGTCACAGTCGGTGATTATTAT
TAACAATTCTACTAATGTTGTTATACGAGCATGTAACCTTTGAATTGTGTGACAACCTTTCTTTGCTGTT
TCTAAACCCATGGGTACACAGACACATACTATGATATTCGATAATGCATTTAATTGCACTTTCGAGTACA
TATCTGATGCCTTTTCGCTTGATGTTTCAGAAAAGTCAGGTAATTTTAAACACTTACGAGAGTTTGTGTT
TAAAAATAAAGATGGGTTTCTCTATGTTTATAAGGGCTATCAACCTATAGATGTAGTTCGTGATCTACCT
TCTGGTTTTTAACACTTTTGAAACCTATTTTTAAGTTGCCTCTTGGTATTAACATTACAAATTTTAGAGCCA
TTCTTACAGCCTTTTCACCTGCTCAAGACATTTGGGGCACGTGAGCTGCAGCCTATTTTGTGGCTATTT
AAAGCCAACTACATTTATGCTCAAGTATGATGAAAATGGTACAATCACAGATGCTGTTGATTGTTCTCAA
AATCCACTTGCTGAACCTCAAATGCTCTGTTAAGAGCTTTGAGATTGACAAAGGAATTTACCAGACCTCTA
ATTTTCAGGGTTGTTCCCTCAGGAGATGTTGTGAGATTCCCTAATATTACAACTTGTCCTTTTGGAGA
GGTTTTTAATGCTACTAAATTCCTTCTGTCTATGCATGGGAGAGAAAAAAATTTCTAATTGTGTTGCT
GATTACTCTGTGCTCTACAACTCAACATTTTTTTCAACCTTTAAGTGCTATGGCGTTTCTGCCACTAAGT
TGAATGATCTTTGCTTCTCCAATGTCTATGCAGATTCTTTTGTAGTCAAGGGAGATGATGTAAGACAAAT
AGCGCCAGGACAAACTGGTGTTATTGCTGATTATAAATTATAAATTGCCAGATGATTTTCATGGGTTGTGTC
CTTGCTTGGAACTAGGAACATTGATGCTACTTCAACTGGTAATTATAAATTATAAATTATAGGTATCTTA
GACATGGCAAGCTTAGGCCCTTTGAGAGAGACATATCTAATGTGCCTTTCTCCCTGATGGCAAACCTTG
CACCCACCTGCTCTTAATTGTTATTGGCCATTAAATGATTATGGTTTTTACACCACTACTGGCATTGGC
TACCAACCTTACAGAGTTGTAGTACTTTCTTTTGAACCTTTTAAATGCACCGGCCACGGTTTGTGGACCAA
AATTATCCACTGACCTTATTAAGAACCAGTGTGTCAATTTTAAATTTTAAATGGACTCACTGGTACTGGTGT
GTTAACTCCTTCTTCAAAGAGATTTCAACCATTTCAACAATTTGGCCGTGATGTTTCTGATTTCACTGAT
TCCGTTTCGAGATCCTAAAACATCTGAAATATTAGACATTTACCTTGCTCTTTTGGGGGTGTAAGTGTA
TTACACCTGGAACAAATGCTTCATCTGAAGTTGCTGTTCTATATCAAGATGTTAACTGCACTGATGTTTC
TACAGCAATTCATGCAGATCAACTCACACCAGCTTGGCGCATATATTCTACTGGAAACAATGTATTCAG
ACTCAAGCAGGCTGTCTTATAGGAGCTGAGCATGTGCACACTTCTTATGAGTGCGACATTCCTATTGGAG
CTGGCATTTGTGCTAGTTACCATACAGTTTCTTTTATACGTAGTACTAGCCAAAAATCTATTGTGGCTTA
TACTATGTCTTTAGGTGCTGATAGTTCAATTGCTTACTCTAATAACACCATTGCTATACCTACTAACTTT
TCAATTAGCATTACTACAGAAGTAATGCCTGTTTCTATGGCTAAAACCTCCGTAGATTGTAATATGTACA
TCTGCGGAGATTCTACTGAATGTGCTAATTTGCTTCTCCAATATGGTAGCTTTTGCACACAACCTAAATCG
TGCACTCTCAGGTATTGCTGCTGAACAGGATCGCAACACACGTGAAGTGTTGCTCAAGTCAAACAAATG
TACAAAACCCCAACTTTGAAATATTTTGGTGGTTTTAATTTTTTCAAAATATTACCTGACCCCTCTAAAGC
CAACTAAGAGGTCTTTTATTGAGGACTTGCTCTTTAATAAGGTGACACTCGCTGATGCTGGCTTCATGAA
GCAATATGGCGAATGCCTAGGTGATATTAATGCTAGAGATCTCATTGTGCGCAGAAGTTCAATGGACTT
ACAGTGTGGCACTCTGCTCACTGATGATATGATTGCTGCCTACACTGCTGCTCTAGTTAGTGGTACTG
CCACTGCTGGATGGACATTTGGTGCTGGCGCTGCTCTTCAAATACCTTTTGTCTATGCAAAATGGCATATAG
GTTCAATGGCATTGGAGTTACCCAAAATGTTCTCTATGAGAACCAAAAACAAATCGCCAACCAATTTAAC
AAGGCGATTAGTCAAATCAAGAATCACTTACAACAACATCAACTGCATTGGGCAAGCTGCAAGACGTTG
TTAACCAGAATGCTCAAGCATTAACACACTTGTAAACAACCTTAGCTCTAATTTTGGTGAATTTCAAG
TGTGCTAAATGATATCCTTTTCGCGACTTGATAAAGTCGAGGCGGAGGTACAAATTGACAGGTTAATTACA
GGCAGACTTCAAAGCCTTCAAACCTATGTAACACAACAACCTAATCAGGGCTGCTGAAATCAGGGCTTCTG
CTAATCTTGCTGCTACTAAAATGTCTGAGTGTGTTCTTGGACAATCAAAAAGAGTTGACTTTTGTGGAAA
GGGCTACCACCTTATGTCCTTCCCACAAGCAGCCCCGCATGGTGTGTCTTCTACATGTCACGTATGTG
CCATCCCAGGAGAGGAACCTCACCCACAGCGCCAGCAATTTGTGTCATGAAGGCAAAGCATACTTCCCTCGT
AAGGTGTTTTTGTGTTTAAATGGCACTTCTTGGTTTTATTACACAGAGGAACCTTTTTCTCCACAAATAAT
TACTACAGACAATACATTTGTCTCAGGAAATTGTGATGTCGTTATTGGCATCATTAACAACACAGTTTTAT
GATCCTCTGCAACCTGAGCTCGACTCATTCAAAGAAGAGCTGGACAAGTACTTCAAAAATCATACATCAC
CAGATGTTGATCTTGGCGACATTTCAAGCATTAACGCTTCTGTGTCGTCACATTCAAAAAGAAATTGACCG
CCTCAATGAGGTGCTTAAAAATTTAAATGAATCACTCATTGACCTTCAAGAATTGGGAAAATATGAGCAA
TATATTAAATGGCCTTGGTATGTTTGGCTCGGCTTCATTGCTGGACTAATTGCCATCGTCATGGTTACAA
TCTTGCTTTGTTGCATGACTAGTTGTTGCAGTTGCCTCAAGGGTGCATGCTCTTGTGGTTCTTGCTGCAA
GTTTGATGAGGATGACTCTGAGCCAGTTCTCAAGGGTGTCAAATTACATTACACATAA

FIG. 21

23/23

HR-C Native (SEQ ID NO:48).

| | | | |
|-------------|--------------------|-------------------|-------|
| 1150 | 1161 | 1171 | 1181 |
| DISGINASVVN | I QKEIDRLNE | VAKNLNESLI | DLQEL |
| ga d a d | a d | a d a | d |

HR-C Analogue 1 (SEQ ID NO:67). Modulation of the “a” residue position

| | | | |
|-------------|--------------------|-----------------------------------|-------|
| 1150 | 1161 | 1171 | 1181 |
| DISGINASVVN | I QKEIDRLNE | V <u>I</u> KNLNESLI | DLQEL |

HR-C Analogue 2 (SEQ ID NO:68). Change of Helical propensity

| | | | |
|-------------|------------------------------------|-----------------------------------|-------|
| 1150 | 1161 | 1171 | 1181 |
| DISGINASVVN | I QKEI <u>A</u> RLNE | VAK <u>A</u> LNESLI | DLQEL |

HR-C Analogue 3 (SEQ ID NO:69). Change of Helical propensity and modulation of “a” position

| | | | |
|-------------|------------------------------------|---|-------|
| 1150 | 1161 | 1171 | 1181 |
| DISGINASVVN | I QKEI <u>A</u> RLNE | V <u>I</u> K <u>A</u> LNESLI | DLQEL |

HR-C Analogue 4 (SEQ ID NO:70). Change of Helical propensity

| | | | |
|--|------------------------------------|--|---------------------|
| 1150 | 1161 | 1171 | 1181 |
| DI <u>AA</u> INASV <u>AN</u> | I QKEI <u>A</u> RLNE | VAK <u>A</u> LNESL <u>A</u> | <u>ALQAL</u> |

HR-C Analogue 5 (SEQ ID NO:71). Introduction of lactam

| | | | |
|-------------|---|-------------------|-------|
| 1150 | 1161 | 1171 | 1181 |
| DISGINASVVN | I QKEI <u>E</u> RLN <u>K</u> | VAKNLNESLI | DLQEL |
| | [] | | |

HR-C Analogue 6 (SEQ ID NO:72). Introduction of salt bridge

| | | | |
|-------------|---|-------------------|-------|
| 1150 | 1161 | 1171 | 1181 |
| DISGINASVVN | I QKEI <u>E</u> RLN <u>K</u> | VAKNLNESLI | DLQEL |

HR-C Analogue 7 (SEQ ID NO:73).

| | | | |
|---|---|--------------------------|---------------------|
| 1150 | 1161 | 1171 | 1181 |
| DI <u>EE</u> IN <u>KKV</u> <u>EE</u> | I <u>QKKI</u> <u>EELN</u> <u>K</u> | <u>KAEELNKKLE</u> | <u>ELQKK</u> |

HR-C Analogue 8 (SEQ ID NO:74). Introduction of salt bridges

| | | | |
|----------------------------|---|--------------------------|-------|
| 1150 | 1161 | 1171 | 1181 |
| DISGINASV <u>VE</u> | I <u>QKKI</u> <u>EELN</u> <u>K</u> | <u>KAEELNKKLI</u> | DLQEL |

FIG. 22